of yeast GGPPS complexed with several bisphosphonate inhibitors. Undecaprenyl diphosphate synthase (UPPS), a *cis*-prenyltransferase, produces C_{55}-undecaprenyl diphosphate (UPP) via *cis* double-bond addition. UPP is used for peptidoglycan cell-wall biosynthesis in bacteria. Here, bisphosphonates were tested as inhibitors of UPPS. In the UPPS-inhibitor complexes, four distinct binding sites were observed. The availability of these structures opens up new avenues for the design of novel inhibitors. Finally, dehydrosqualene synthase (CrtM) from *Staphylococcus aureus*, uses the head-to-head condensation of two molecules of farnesyl diphosphate (FPP) to produce the presqualene diphosphate C_{30} molecule, the precursor for of staphyloxanthin, the golden carotenoid pigment which promotes bacterial resistance to reactive oxygen species and host neutrophil-based killing. CrtM, therefore, has been tested as the target to treat infections by methicillin-resistant *S. aureus* (MRSA). We found squalene synthase inhibitors for cholesterol-lowering activity in humans bind to CrtM and block the biosynthesis of staphyloxanthin *in vitro*, resulting in colorless bacteria with increased susceptibility to killing by human blood and to innate immune clearance in a mouse infection model.

I-32 Antibiotic use and epidemiology characteristic of methicillin-resistant *Staphylococcus aureus* in Chinese pediatrics

X.Z. Shen[1]*, W.S. Zhang[1], H. Zhang[2], C.Q. Wang[3], J.H. Zhen[1], Q.L. Deng[4], L. Liu[5], X.H. Wang[3], K.H. Yao[1], S.J. Yu[1], Y.H. Yang[1]. *[1]Beijing Children's Hospital affiliated to Capital Medical University, Beijing, China, [2]Shanghai Children's Hospital affiliated to Shanghai Jiaotong University, Shanghai, China, [3]Children's Hospital affiliated to Fudan University, Shanghai, China, [4]Guangzhou Children's Hospital affiliated to Guangzhou Medical College, Guangzhou, China, [5]Chongqing Children's Hospital affiliated to Chongqing Medical University, Chongqing, China*

The global escalation in both community- and hospital-acquired antimicrobial-resistant bacteria is threatening the ability to effectively treat patients, but there is not enough concern about the antibiotic rational use. Now the antibiotic irrational use and the development of antibiotic resistance have already been a problem threatening public health. This survey included the 5 main children's hospitals in the 4 biggest cities in China, All hospitalized patients aged 0–15 years were included from 2002 to 2005. We have evaluated the use of the systemic antibacterial drugs (ATC-group J01) using the ATC/DDD methodology. Data were expressed as the number of DDD per 100 bed-days of inpatients. The Drug Utilization 90% (DU 90%), were determined. The overall inpatient use of antibiotic drugs was 68.2, 58.4, 65.8, 65.6 and 49.9 DDD/100 bed-days for the years 2002 to 2006, respectively. Beta-lactam antibacterials were the most used subgroups and the top antibiotics used were third-generation cephalosporins of inpatients. The number of antimicrobial agents and non-restricted antibiotics within DU90% segment ranged from 11 to 20 and from five to nine, respectively. Antibiotics that could be injected were used widely in admitted patients and accounted for 59.0%-99.8%. The antibiotic overuse in inpatients was found in this study. It could be the result of the increasing of antimicrobial-resistant pathogens.

The emergence and dissemination of methicillin-resistant *S. aureus* (MRSA) is increasing in prevalence in all regions of Canada, in the United States, and globally. But now, the effect of large-scale expanded surveillance for methicillin-resistant *Staphylococcus aureus* (MRSA) on health care-associated MRSA disease is not known in China. Within the previous two decades, MRSA had been established as a major nosocomial pathogen. In the 1980s, community-associated MRSA (CA-MRSA) infections appeared and their prevalence increased gradually. To investigate the genetic differentiation and pathogenicity of MRSA from Chinese pediatric, seventy-three MRSA isolates were analyzed by a combination of different genotyping methods, including multilocus sequence typing (MLST), SCC *mec* and *spa* typing. Panton-Valentine Leukocin (PVL) gene was also detected. The prevalent strains were ST239-MRSA-III and ST1-MRSA clones in the northern region; ST239-MRSA-III, ST910-MRSA-IV and ST88-MRSA in the eastern region; and ST59-MRSA in the southern region. We also found several novel genetic types. Antimicrobial susceptibility tests showed high resistance of many antimicrobials and multiple drugs. PVL gene-positive MRSA was likely to be associated with the necrotic process in clinical infections.

I-33 Molecular identification and typing of methicillin-resistant *Staphylococcus aureus* (MRSA)

M. Ip*. *The Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong, China*

Methicillin-resistant *Staphylococcus aureus* (MRSA) is a significant cause of healthcare- and community-associated infections. MRSA infections are a major public health concern and its prevalence is increasing globally. Strategies of active surveillance, aggressive patient management, including rigorous infection prevention measures, both in hospital setting and in the community, are necessary in the control of MRSA infections.

Effective strategies in the control of MRSA have been facilitated by the availability of rapid molecular diagnostic methods for the detection and identification of MRSA from MRSA-infected patients and carriers. Successful infection control programs require understanding and reducing transmission of different strain types of MRSA. Hospital and community genotypes of MRSA are often distinct and need to be distinguished in establishing strategies for control. There are pros and cons to the molecular methods available for characterizing these MRSA strains. Methods that are commonly used include pulsed-field gel electrophoresis, multilocus sequence typing (MLST), spa-typing, and detection of staphylococcal *mec* cassette genes (SCC*mec*) and virulence gene targets, such as panton-valentine leukocidin (*pvl*) gene and other toxin genes. Current molecular methods of detection and genotyping of MRSA strains will be discussed.

The cost-effectiveness and clinical efficacy of implementing these technologies depends on the level of clinical service that is available in individual hospitals and requires risk assessments for the control of MRSA in different settings.

I-34 Resistance in *S. aureus*: Should epidemiology patterns influence the choice of therapy?

H. Wang*. *Peking Union Medical College Hospital, 100730, Beijing, China*

Staphylococcus aureus, which causes a wide range of clinical infections, is a prominent pathogen in both the hospital and the community settings. The incidence of methicillin-resistant *S. aureus* (MRSA) has been increasing at an alarming rate in Asia, along with that heterointermediate resistance to vancomycin (hVISA). Previous data indicated that Asia-Pacific had one of the highest prevalence rates of hospital-acquired MRSA (HA-MRSA) that ranged from 50–80%. The prevalence of HA-MRSA in Mainland China was only 27.8% in 1999, however, in 2005, the prevalence reached to 50.3%. The genotypic characteristics of HA-

MRSA strains in most Asian region were ST239-MRSA-SCCmecIII except for those from Korea and Japan which were ST5-MRSA-SCCmecII. In Mainland China, our study showed the most predominant types were ST239-SCCmecIII and ST5-SCCmecII, which accounted for 75.5% and 17.0%, respectively. The prevalence of pvl gene in all *S. aureus* varied among different regions. Several studies indicated that CA-MRSA had been emerging in Asia. A recent study in China Hong Kong demonstrated 10.4% of *S. aureus* isolates from patients with purulent skin and soft tissue infections (SSTIs) were attributed to pvl-positive CA-MRSA. The molecular characteristics of CA-MRSA showed different patterns between regions, In Asia, strains in Singapore was ST30-MRSA-SCCmecIV, in Hong Kong was ST30-MRSA-SCCmecIV, ST59-MRSA-SCCmecV and ST8-MRSA-SCCmecIV, in Taiwan was ST59-SCCmecIV, while in Korea, was ST72-SCCmec type IV. Our finding showed two isolates of CA-MRSA were found in Mainland China, one with ST88-SCCmec IV, the other one with ST59-SCCmec IV. A study conducted by ANSORP Study Group showed that *Staphylococcus aureus* with reduced susceptibility to vancomycin existed in Asia. The prevalence of hVISA was 4.3%, the highest in Japan (8.2%). In our recent study we found the vancomycin MIC was elevated. In Asia, notable high prevalence of MRSA was observed. This is consistent with the establishment and gradual spread within countries of distinct MRSA clones that are highly resistant to common antibiotics, perhaps favored by the relative geographic isolation of some contributors. And the epidemiology patterns will surely complicate the choice of therapy, and make it much harder.

Concurrent Session 6 – Tuberculosis Updates

I-35 Extensively drug resistant tuberculosis (XDR-TB) – An overview

R.C. Read*. *University of Sheffield, UK*

Extensively drug resistant tuberculosis (XDR-TB) is defined as tuberculosis caused by a *Mycobacterium tuberculosis* strain which is resistant to Rifampicin and isoniazid (i.e. multidrug-resistant tuberculosis – MDRTB), but in addition is resistant to a fluoroquinolone, plus at least one injectable second-line anti-tuberculous drug (i.e. one of amikacin, kanamycin and/or capreomycin). The World Health Organisation has established sentinel reference laboratories throughout the world and XDR-TB strains are being identified in all continents with a worldwide prevalence in the region of 7% amongst MDRTB strains. Recent studies in Southern Africa have demonstrated the very high mortality associated with XDR-TB especially in patients co-infected with human immunodeficiency virus. Therapeutic options are extremely limited. The emergence of XDR-TB is a reflection of failure to manage compliance of tuberculosis chemotherapy coupled with failure to follow international therapeutic guidelines. Managing cases is exceptionally complex and requires specialised facilities and therapeutics. Controlling the emergence of XDR-TB will require a concerted and urgent global public health response, particularly in developing countries with limited resources and those countries with high rates of sero-prevalence of HIV.

I-36 Latent infection of *M. tuberculosis* in China

W.H. Zhang*. *Department of Infectious diseases, Huashan Hospital, Fudan University, Shanghai, 200040, China*

Background and Objectives: Tuberculosis (TB) is the second leading cause of death worldwide, killing around 1.8 million persons annually. Despite well-implemented DOT in China, cases of active tuberculosis keep increasing. According to the report from Chinese government, annual new pulmonary TB cases increased by 29% from 0.97 million in year 2004 to 1.25 million in year 2005. However, the disease burden of latent infection of M. tb and its contribution to new cases of tuberculosis are still unclear in China and there has been no formal reports describing the incidence of latent tuberculosis infection (LTBI) conversion to active TB. Meanwhile, The immune mechanisms for LTBI conversion to active TB remain poorly characterized. The objective of this study is to describe the prevalence of latent tuberculosis infection (LTBI) in high risk populations in China and explore the mechanisms of conversion to active TB from LTBI.
Methods and Results: We have designed a cross-section study including 3 groups of persons at high risk, including house contacts to TB cases and HIV positive patients. Using the rapid ELISPOT assay, we enumerated T-cells specific for ESAT-6 and CFP-10 in blood samples from 194 household contacts of these tuberculosis cases and 100 HIV positive cases. Intracellular cytokine staining (ICS) were employed to detect the changes of numbers and function of T lymphocytes in all subpopulations. The results showed that a 48.96% prevalence of latent *M. tuberculosis* infection in China in high risk populations who have intimate contact with patients with active tuberculosis. Meanwhile the prevalence of latent *M. tuberculosis* infection in HIV positive cases is up to 59%. The percentage of CD3+CD4+ and CD3+CD8+ cells and their subsets in CD3+ T-cells in peripheral blood is decreased dramatically in HIV positive cases with infection or latent infection of *M. tuberculosis.*
Conclusions: 1. ELISPOT assay is a more sensitive assay for detection of active pulmonary TB without treatment than conventional tools. It is more specific, and possibly more sensitive, than PPD-based methods of detecting latent *M. tuberculosis* infection in China. 2. The disease burden of latent infection of *M. tuberculosis* is heavy in China and whether it is of high priority to treat LTBI in China to boost the decline of TB pandemics under the DOTS program remains to be determined. 3. The results also shows CD3+CD4+, CD3+CD8+ and $V\gamma2V\delta2$+ T-cells may all contribute to the immune protection against the mycobacterial infection and is highly associated with the conversion from latent infection to active infection of *M. tuberculosis*.

I-37 Epidemiology of *Mycobacterium tuberculosis* genotypes in different ethnic and age populations in Taiwan

I.J. Su*, H.Y. Dou. *Division of Clinical Research, National Health Research Institutes, Tainan, Taiwan*

Aims: The distribution of human *Mycobacterium tuberculosis* (MTB) genotypes is closely associated with geography, ethnicity, age and host factors. This study is designed to study the molecular epidemiology of MTB in Taiwan with emphasis on the ethnicity and migratory history (Part I). The distribution of MTB genotypes in metropolitan Taipei city was further analyzed with specific emphasis on the clustering and age association (Part II).
Methods and Results: *Part I study:* Three groups of 208 patients with tuberculosis in Taiwan were sampled to test this observation: (1) 41 aborigines of Austronesian ethnicity, who have been inhabiting in Taiwan for more than 500 years; (2) 58 veterans of Han Chinese origin, who moved as the first generation from Mainland China to Taiwan 55–60 years ago; and (3) 109 patients representing the general Taiwanese population of Han Chinese whose ancestors migrated to Taiwan around 200–400 years ago. A total of 208 MTB isolates, one per patient, were analyzed by